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## PATENT COOPERATION TREATY



Translation

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 345586 D20785	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR2003/003651	International filing date (day/month/year) 10 décembre 2003 (10.12.2003)	Priority date (day/month/year) 10 décembre 2002 (10.12.2002)
International Patent Classification (IPC) or national classification and IPC A61K 35/78, 7/48		
Applicant BAYER CONSUMER CARE AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.
<input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items: <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand 01 juillet 2004 (01.07.2004)	Date of completion of this report 17 March 2005 (17.03.2005)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR2003/003651

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
 pages \_\_\_\_\_ 1-50 \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
 pages \_\_\_\_\_ 1-23 \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, as amended (together with any statement under Article 19  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
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## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	1-23	YES
	Claims		NO
Inventive step (IS)	Claims	1-23	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-23	YES
	Claims		NO

## 2. Citations and explanations

Reference is made to the following documents:

- D1: DATABASE WPI Section Ch, Week 199239 Derwent Publications Ltd., London GB; Class B04, AN 1992-321310 XP002251031 & KR 9 102 518 B (DONG KUK PHARM CO) 23 April 1991 (1991-04-23);
- D2: EP-A-0 867 447 (DONG KOOK PHARM CO LTD) 30 September 1998 (1998-09-30);
- D3: DATABASE BIOSIS [on line], BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1992, COLLINS D J ET AL: "TRITERPENE ACIDS FROM SOME PAPUA NEW GUINEA TERMINALIA SPECIES" XP002251030 Database Accession no. PREV199293116315.

*Novelty*

D1 and D2 disclose extraction methods based on the *Centella asiatica* plant. Said methods differ from the methods claimed in claims 1 and 2 (at least) in that they do not include steps (c) and (e). Document D3 relates to ether extracts and is not, therefore, considered to be

relevant.

The description does not cite any documents reflecting the prior art described on page 3, lines 16-23 (contrary to PCT Rule 5.1(a)(ii)). This prior art relates to extraction methods that lead to a mixture of asiaticoside, madecassoside and secondary substances (15%), or 81% of madecassoside and isomers close to madecassoside.

The subject matter of claims 1 and 2 relates to methods for preparing a *Centella asiatica* extract containing, *inter alia*, madecassoside and terminoloside.

Terminoloside is a position isomer of madecassoside (the present description, page 4, line 15). The methods cited above include a non-negligible amount of impurities that could be terminoloside owing to the structure thereof, which is close to that of madecassoside. In the absence of any more specific information on the various steps of the prior art methods and the content of the extracts resulting from said methods, in particular, the presence of amounts of terminoloside, the subject matter of claims 1 and 2 is considered to be novel.

The same reservations are made with respect to the product claims (claims 9, 12, 15 and 22). As far as the novelty of claims 9, 12, 15 and 22 is concerned, it should be noted that document D3 (the abstract, last sentence) casts doubt on the presence of glycosides of terminolic acid in the *Centella asiatica* extracts and contradicts the passage on page 4, lines 15-17 ("terminoloside has never been cited as being a possible extract of *Centella asiatica*"). For these reasons, the subject matter of claims 9, 12, 15 and 22 can be considered to be novel.

*Inventive step*

Documents D1 and D2, or even the references cited on page 3, lines 16-23, of the present description, are considered to be the closest prior art and it would appear that the difference between the prior art extraction methods and the invention as claimed is the presence of terminoloside. The technical problem to be solved is defined as being that of providing methods for extracting terminoloside.

In view of the fact that D3 casts serious doubt on the presence of terminolic acid in *Centella asiatica* extracts and that, in comparison with the extraction methods described in D1 and D2, two method steps must be modified, the subject matter of claims 1 and 2 can be considered to be inventive.

The presence of terminoloside in *Centella asiatica* extracts (that contain, *inter alia*, madecassoside and asiaticoside as active substances) gives rise to a technical effect (see pages 46 and 48, which describe the effects on IL-1 and PGE-2 production). It follows that not only can the method be considered to be inventive, so too can the resulting product. As a result, the subject matter of claims 9, 12, 15, 22 and 23 also involves an inventive step.